REMARKS

The invention relates in part to assay devices that utilize mass transport by laminar flow of a sample through the layers of the device. Because laminar flow overcomes limitations in sensitivity caused by diffusion boundary formation as an analyte binds to a surface, the devices of the present invention can provide advantageous capture efficiencies.

Claims 1-50 are currently pending in the instant application with claims 13-17 and 35 having been withdrawn from consideration by the Examiner in a restriction requirement. Claims 1-6, 18, 19, 23, 36, 42, and 43 are amended herein. The amended claims are fully supported by the specification, and do not introduce new matter or require a new search. Exemplary support for the amended language can be found in the specification as follows:

"a fluid sample"	the use of fluid samples is described on page 9, line 5.
"providing an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding"	As described on page 10, lines 4-23, the term "optically functional layer" refers to a layer that can produce a signal upon binding of an analyte to a receptive layer on the optically functional layer. Generation of the signal is due to changes in one or more optical properties of the optically functional layer. Examples of such changes in optical properties include attenuation of one or more wavelengths of light; extinction or enhancement of specific wavelengths; modification of intensity of specific wavelengths; or modification of the state or degree of polarization, *etc.* As described on page 8, lines 15-18, and page 15, line 9, through page 16, line 2, this change in optical properties is mediated by a mass change on the optically functional layer that is related to analyte binding.

optically functional layers, attachment layers, and/or analyte specific receptive layers that "are configured and arranged to provide channels through each of said layers that are continuous with said channels in said support"	As described on page 5, line 28, through page 6, line 1, the optically functional layer is applied to the channel containing support in a manner that maintains the support channels. Page 35, lines 3-4 notes that the attachment layer does not have an appreciable effect on these channels. The optional analyte specific receptive layer is attached to the attachment layer materials.
attachment layers, and/or analyte specific receptive layers that "are configured and arranged to provide channels through each of said layers that are continuous with said channels in said optically functional layer"	As described on page 13, lines 1-9, the device may comprise a porous, rather than a channeled, support, and the optically functional layer may contain channels. Page 35, lines 3-4 notes that the attachment layer does not have an appreciable effect on these channels. The optional analyte specific receptive layer is attached to the attachment layer materials.

Notwithstanding the foregoing, Applicants expressly reserve the right to pursue subject matter no longer claimed in the instant application in one or more applications which may claim priority hereto. Applicants respectfully request reconsideration of the claimed invention in view of the foregoing amendments and the following remarks.

Non Art-Related Remarks

Telephonic Interview

The courtesy extended to Dr. Diana Maul and Applicants' representative in the telephonic interview conducted by Examiner Marschel on January 14, 2003 is gratefully acknowledged and appreciated.

Title

The Examiner has requested a new title be provided for the present invention. Applicants suggest the following for the Examiner's consideration:

"Flow-through optical assay devices providing laminar flow of fluid samples"

Applicants respectfully request that the Examiner approve the foregoing change to the title of the application.

35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse in part the rejection of claims 1-12, 18-34, 36-40, and 42-50 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention..

When determining definiteness, the proper standard to be applied is "whether one skilled in the art would understand the bounds of the claim when read in the light of the specification." *Credle v. Bond*, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). See also *Miles Laboratories, Inc. v. Shandon, Inc.*, 27 USPQ2d 1123, 1127 (Fed. Cir. 1993) ("If the claims read in the light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.") (emphasis added).

Applicants respectfully disagree with the contention that the phrase "laminar flow of sample" is allegedly unclear as to whether a sample is present in the claimed devices. Nevertheless in an effort to advance prosecution, Applicants have amended claims to clarify that the devices are configured and arranged to provide laminar flow when a fluid sample is introduced into the device. This amendment is intended to clearly indicate to the skilled artisan that a sample is not a required element of the device; rather, the amended phrase describes structural elements of the claimed device that are designed to provide a specific functional result. Applicants submit that the foregoing amendments render the rejection moot, and respectfully request that the rejection be withdrawn.

With regard to the Examiner's objections to claims 18, 36, 42, and 43, Applicants submit that the foregoing amendments render the rejection moot, and respectfully request that the rejection be withdrawn.

Applicants respectfully traverse the Examiner's rejection of claims 2, 4, 6-12, 19-22, 36-40, and 44-50. The Examiner's contention that the claims refer to assay devices, but the claims refer to nothing in the devices that interact with an analyte (e.g., the "analyte specific receptive layer" of claim 1) is incorrect. As described in detail in the instant specification, in certain embodiments the attachment layer provides nonspecific capture of the analyte. In these embodiments, specific identification of the analyte is performed by the later addition of an

analyte-specific reagent, and the change in mass on the optically functional layer that is detected is related to binding of this analyte-specific reagent. *See, e.g.*, specification, page 34, lines 19-27.

Based on the foregoing, the skilled artisan would understand that, in the devices that do not specifically recite the presence of an analyte specific receptive layer, the open "comprising" form of the claim would encompass devices that nonspecifically bind the analyte, as well as devices that further comprise an analyte specific receptive layer. Nevertheless, in an effort to advance prosecution, Applicants have amended those claims to which the Examiner objects to recite that the attachment layer provides nonspecific binding of the analyte. Applicants submit that the foregoing amendments render the rejection moot, and respectfully request that the rejection be withdrawn.

Art-Related Remarks

35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 1, 2, 5, 6, 9, 18-20, 22-24, 26, and 36 under 35 U.S.C. § 102(b) as allegedly being anticipated by Brecht *et al.*, Anal. Chim. Acta 311: 289-299 (1995).

In order to anticipate a claim, a single prior art publication must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the teachings of the specification. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). *See* also MPEP §2131.

As discussed in Applicants' previous responses, the Brecht *et al.* publication does not provide any devices in which laminar flow is provided, as required by the instant claims. The Examiner now disagrees with the previous position of the Office, *e.g.* discussed in Paper No. 11, part 2, in which the Examiner conceded that cells disclosed in the Brecht *et al.* publication are not true "laminar flow" cells, and thus do not provide laminar flow as recited in the instant claims. Paper No. 26, page 7. The Examiner, however, has not rebutted the evidence provided by Applicants regarding the nature of flow in the devices disclosed by the Brecht *et al.* publication; rather, the Examiner simply states that "Brecht et al., clearly disclose a laminar flow cell." Paper No. 26, page 8. Applicants reiterate that, despite using the words "laminar flow," the devices disclosed by the Brecht *et al.* publication do not provide laminar flow, and respectfully request

that the Examiner indicate why Applicants' evidence is deficient should the rejection be maintained.

Moreover, As noted by Applicants previously, even if "laminar flow" is provided by the devices disclosed in the Brecht *et al.* publication, reagent flow in such devices does not occur through the layers of the device, but rather across a device surface from an inlet port to an outlet port. See, e.g., Brecht *et al.*, page 292, "Setup" (a "chip" comprising interference layers as mounted on a flow cell; in the "laminar" flow cell, inlet and outlet are on the sides of the cell, and no channels are present on the "chip").

In the telephonic interview, the Examiner indicated that the claims should make clear that the channels of the support material are maintained through the various layers of the instantly claimed devices. In response, Applicants have amended the claims herein to recite that, in devices in which the support is a channeled support, the optically functional layer, attachment layer, and analyte specific receptive layer (when present) provide channels through each layer that are continuous with the channels in the support; likewise, in devices in which the support is porous and the optically functional layer contains channels, the attachment layer and analyte specific receptive layer (when present) provide channels through each layer that are continuous with the channels in the optically functional layer.

Because Brecht *et al.* publication does not teach each and every element set forth in the claims, no *prima facie* case of anticipation has been established. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 1, 2, 5, 6, 9, 18-20, 22-24, 26 and 36 under 35 U.S.C. §103(a), as allegedly being unpatentable over Oberhardt, U.S. Patent No. 4,849,340 ("the '340 patent").

To establish a *prima facie* case of obviousness, three criteria must be met: there must be some motivation or suggestion, either in the cited publications or in knowledge available to the ordinarily skilled artisan, to modify or combine the publications; there must be a reasonable expectation of success in combining the publications; and the publications must teach or suggest

all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) See also MPEP §2143.

As noted previously by Applicants, the "optically functional layer" defined in the instant application refers to a layer that contains the active components required to produce a signal by a modification of the optical properties of the surface resulting solely from binding of material to the surface, and not through the use of labeled species such as fluorescent molecules. *See*, specification page 10, lines 4-23. Thus, when properly interpreted, it is clear that no optically functional layer is disclosed or suggested by the '340 patent.

The Examiner contends that a statement regarding the meaning of a term set forth in the file history need not be considered in interpreting a claim term. Paper No. 26, page 11. Applicants respectfully request that the Examiner cite some support for this proposition should the rejection be maintained. As stated in *Vitronics Corp. v. Conceptronic Inc.*, 39 USPQ2d 1573, 1576 (Fed. Cir. 1996), "Although the words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history" (emphasis added).

In the telephonic interview, the Examiner indicated that the claims should make clear that the optically functional layer is defined in this manner. In response, Applicants have amended the claims herein to recite that the claimed devices comprise "an optically functional layer, an optical property of which is detectably altered upon a change in mass on the optically functional layer related to analyte binding."

Furthermore, as recognized by the Examiner (Paper No. 23, page 6), the '340 patent does not disclose laminar flow through the reflective surface. While the Examiner contends that "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to optionally construct and utilize a device with laminar flow through various layer selections because the '340 patent alleged to describe a wide variety of optically functional layers as well as supports, channels, analyte attachment layers, etc.," this unsupported assertion by the Examiner lacks a key element of any obviousness rejection -- a motivation to perform the modification suggested by the Examiner.

The Examiner responds by stating that "a generic disclosure of clearly set forth options is deemed... to motivate and suggest the selection of any of the options." Paper No. 26, page 12. Applicants respectfully submit that nowhere in the '340 patent is the concept of laminar flow disclosed, generically or otherwise. In the absence of objective evidence providing a motivation to modify the devices disclosed in the '340 patent to the instantly claimed devices, no *prima facie* case of obviousness has been established.

Because the '340 patent fails to teach or suggest all of the limitations set forth in the instant claims, and because nothing in the Examiner's asserted *prima facie* case provides any motivation to modify the devices of the cited patent to provide the instantly claimed invention, Applicants respectfully request that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn.

Applicants also respectfully traverse the rejection of claims 1, 2, 5, 6, 9, 18-20, 22-24, 26 and 36 under 35 U.S.C. §103(a), as allegedly being unpatentable over Walt *et al.*, U.S. Patent No. 6,023,540 ("the '540 patent").

Applicants noted previously that the present application claims priority to U.S. Patent Application No. 08/742,255, which was filed on October 31, 1996. As such, the cited publication, filed on March 14, 1997, is not prior art to the present application.

In response, the Examiner states that Applicants have not provided factual support such as pointing to support for the present claims in the parent application, and that the Examiner identified no support in the parent application for the present claims. Paper No. 26, page 12-13.

Applicants respectfully submit that claims 1-36 as originally filed in the present application are identical to claims 1-36 as originally filed in the parent application. With regard to the amendments made in the present submission, identical exemplary support for the amended language can be found in the parent specification as was discussed above for the instant specification:

"a fluid sample"	the use of fluid samples is described on page 9, line 5.
"providing an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding"	As described on page 10, lines 4-23, the term "optically functional layer" refers to a layer that can produce a signal upon binding of an analyte to a receptive layer on the optically functional layer. Generation of the signal is due to changes in one or more optical properties of the optically functional layer. Examples of such changes in optical properties include attenuation of one or more wavelengths of light; extinction or enhancement of specific wavelengths; modification of intensity of specific wavelengths; or modification of the state or degree of polarization, *etc.* As described on page 8, lines 15-18, and page 15, line 14, through page 16, line 7, this change in optical properties is mediated by a mass change on the optically functional layer that is related to analyte binding.
optically functional layers, attachment layers, and/or analyte specific receptive layers that "are configured and arranged to provide channels through each of said layers that are continuous with said channels in said support"	As described on page 5, line 28, through page 6, line 2, the optically functional layer is applied to the channel containing support in a manner that maintains the support channels. Page 31, lines 16-17 notes that the attachment layer does not have an appreciable effect on these channels. The optional analyte specific receptive layer is attached to the attachment layer materials.
attachment layers, and/or analyte specific receptive layers that "are configured and arranged to provide channels through each of said layers that are continuous with said channels in said optically functional layer"	As described on page 13, lines 5-13, the device may comprise a porous, rather than a channeled, support, and the optically functional layer may contain channels. Page 31, lines 16-17 notes that the attachment layer does not have an appreciable effect on these channels. The optional analyte specific receptive layer is attached to the attachment layer materials.

In view of the foregoing, Applicants respectfully submit that the cited publication is not prior art to the present application and request that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn.

Obviousness-type double patenting

The Examiner has provisionally rejected claims 1, 2, 5-12, 23, 24, 26-34, and 36-50 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 51, 52, 54, 55, 57-63, 66-68, 70, 71, 73-79, and 82 of copending U.S. Application No. 09/675,518. Applicants respectfully submit that, because the instant claims are in allowable form, the provisional double patenting rejection is the only remaining rejection in the instant application. As such, the examiner should withdraw the rejection and permit the claims to issue. *See, e.g.*, MPEP 804(I)(B).

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the address and telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,
FOLEY & LARDNER

Dated: February 7, 2003

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1. (Three times amended) An optical assay device for the detection of an analyte of interest in a fluid sample comprising:

a support containing channels;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, positioned on said support;

an attachment layer positioned on said optically functional layer; and

an analyte specific receptive layer positioned on said attachment layer,

wherein said support, optically functional layer, attachment layer, and analyte specific receptive layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said support, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when a fluid sample is introduced into said device.

2. (Three times amended) An optical assay device for the detection of an analyte of interest in a fluid sample comprising:

a support containing channels;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, positioned on said support; and

an attachment layer positioned on said optically functional layer,

wherein said support, optically functional layer, and attachment layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said support, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when said fluid sample is introduced into said device.

3. (Three times amended) An optical assay device for the detection of an analyte of interest in a fluid sample comprising:

a porous support;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, comprising discrete, optically functional particles embedded in said support configured and arranged to provide channels through said optically functional layer;

an attachment layer positioned on said particles; and

an analyte specific receptive layer positioned on said attachment layer,

wherein said [support] attachment layer and analyte specific receptive layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said optically functional layer, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when said fluid sample is introduced into said device.

4. (Three times amended) An optical assay device for the detection of an analyte of interest in a sample comprising:

a porous support;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, comprising discrete, optically functional particles embedded in said support configured and arranged to provide channels through said optically functional layer; and

an attachment layer positioned on said particles,

wherein said [support] attachment layer is configured and arranged (i) to provide channels through [and] said attachment layer that are continuous with said channels in said optically functional layer, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when said fluid sample is introduced into said device.

5. (Three times amended) An optical assay device for the detection of an analyte of interest in a sample comprising:

a porous support;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, containing channels positioned on said support;

an attachment layer positioned on said optically functional layer; and

an analyte specific receptive layer positioned on said attachment layer,

wherein said [support] attachment layer and analyte specific receptive layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said optically functional layer, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when said fluid sample is introduced into said device.

6. (Three times amended) An optical assay device for the detection of an analyte of interest in a sample comprising:

a porous support;

an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, containing channels positioned on said support; and

an attachment layer positioned on said optically functional layer,

wherein said [support] attachment layer is configured and arranged (i) to provide channels through [and] said attachment layer that are continuous with said channels in said optically functional layer, and (ii) [are configured and arranged] to provide laminar flow of sample [flow] through each of said layers [via said channels] of said device when said fluid sample is introduced into said device.

18. (Four times amended) Method for constructing an optical assay device with laminar flow properties, comprising the steps of:

providing a support comprising channels;

providing an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, on said support;

providing an attachment layer on said optically functional layer; and

providing an analyte specific receptive layer on said [optically functional] attachment layer,

wherein said support, optically functional layer, attachment layer, and analyte specific receptive layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said support, and (ii) [are configured and arranged] to provide laminar flow of sample through each of said layers [via said channels] or through each of said layers [via said channels] and across one or more of said layers of said device when said fluid sample is introduced into said device.

19. (Four times amended) Method for constructing an optical assay device with laminar flow properties, comprising the steps of:

providing a support comprising channels;

providing an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding, on said support; and

providing an attachment layer on said optically functional layer,

wherein said support, optically functional layer, and attachment layer are configured and arranged (i) to provide channels through [and] each of said layers that are continuous with said channels in said support, and (ii) [are configured and arranged] to provide laminar flow of sample through each of said layers [via said channels] or through each of said layers [via said channels] and across one or more of said layers of said device when said fluid sample is introduced into said device.

23. (Three times amended) A composition comprising:

a support comprising channels, and an optically functional layer, an optical property of which is detectably altered upon a change in mass on said optically functional layer related to analyte binding,

wherein said optically functional layer is configured and arranged (i) to provide channels through said optically functional layer that are continuous with said channels in said support, and (ii) to provide laminar flow of sample through said optically functional layer towards said support [via said channels] when a fluid sample is introduced onto said optically functional layer.

36. (Amended) The device of any of claims 1, 2, 3, 4, 5 or 6, wherein said analyte is selected from the group consisting of antigens, antibodies, receptors, ligands, chelates, proteins, enzymes, nucleic acids, DNA, RNA, pesticides, and herbicides[, inorganic or organic compounds].

39. An assay device for the detection of an analyte of interest comprising:

a support, [and]

an optically functional layer positioned on said support, and

an attachment layer positioned on said support to provide nonspecific capture of said analyte, said attachment layer comprising diamond-like carbon.

40. An optical assay device for the detection of an analyte of interest comprising:

a support,

an optically functional layer positioned on said support, [and]

an attachment layer positioned on said optically functional layer comprising diamond-like carbon, and

an analyte specific receptive layer positioned on said attachment layer.

42. (Amended) The device of claim 39 or 40, wherein said attachment layer non-specifically binds analyte selected from the group consisting of antigens, antibodies, receptors, nucleic acids, polysacchrides, lipopolysacchrides, enzymes, proteins, microorganisms, fragments derived from microorganisms, haptens, drugs, food contaminants, environmental agents, ligands, and chelators[, and analogs or derivatives thereof].

43. (Amended) The device of claim 41, wherein said receptive layer comprises biomolecules selected from the group consisting of antigens, antibodies, receptors, nucleic acids, polysacchrides, lipopolysacchrides, enzymes, proteins, microorganisms, fragments derived from microorganisms, haptens, drugs, food contaminants, environmental agents, ligands, and chelators[, and analogs or derivatives thereof].